- Nikita Ma'am

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◀◀◀◀◀ REPRESENT YOUR SELF ▶▶▶▶▶

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Class D- Pharma
Section
Subject Pharmaceutic

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Chap-1

Dose:- it is a quantity of the drug required to produce the desired action.

Doses form:- the drug is combined with non-drug component (additive) and the resulting form of drug is known as doses form.

Additive:- the non-drug components which are mixed with the drug to form a suitable doses form is called additive.

Drug:- a drug may be defined as an agent intended for use in mitigation, treatement, cure or prevention of disease in man or an animal & they may be used internally or externally.

Drug = API + Excipients

Pharmaceutics:- it is the branch of pharmacy which deals with the formulation, manufacturing, evaluation, packaging and storage of pharmaceutical does form.

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History of profession of pharmacy in India in

relation to pharmacy, education, industry, pharmacy practice & various professional association

1. The word pharmacy is originated from greek world Pharmakon which means both drug & poison.

2. It was in 9th century in Baghdad that the profession of pharmacy started accuring shape.

3. 1901 stablishment of the Bengal Chemical pharmaceutical by Professor P.C. Ray.

4. 1903 discovered a small factory at Bombay established by T.K. Gujjar.

Indian System Of Medicine

1. In ancient India the source of vegetable, animals and marine that was known as Ayurvedic system, they were prepared by experienced person.

2. Knowledge of that medicine was kept secret within a family.

3. There was no scientific method of preparation & standard of medicine.

Muslim Rule in India

1. The Indian System of medicine declined during the muslim rule.

2. Yunani system of medicine is a great healing art as well as science. It treats a person as a whole not as a group of individual part. It is aimed act treating body, mind and soul.

3. The system is based on hypocrating theory.

British Rule in India

1. The western or Alopathic system came into India when britishers became the ruler.

2. Before 1940 initially all the drugs were imported from Europe, later some drug begin to be manufactured in India

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Introduction to Pharmacopoeia.

The word pharmacopoeia comes from Greek word pharmakon which means 'drug or poison' and poein means 'to make' and the combination means 'any recipe or formula or other standard required to make a drug'.

The term pharmacopoeia was used firstly in 1580 in a book on drug standards printed in Bergambo, Italy.

After that a number of national pharmacopoeia were published various Europian countries. Each pharmacopoeia were published by Europian countries. Each P. copoeia describe different strength & method of preparation.

To overcome this difficulty the first British P. copoeia came into existance in 1864

In the United States, the first P. copoeiaa was published by WHO in 1951 (Volume I) and in 1955 (Volume 2)

[DTAB - Drug Technical Advisory Board]

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History of Pharmacopoeia in India

The government of India directed DTAB (drug technical advisiary board) to list the drugs used in India and also recommend the standards to be prescribed to maintain uniformity and chemical test to be used to established identity & purity.

The Indian P. copoeia list contains about 180 monograph and a number of 100 monograph ~~were~~ work on ~~all~~ vegetable drugs growing in India. The drug of plant origin such as bael, berries, cannabis, punarnawa, rawolfia were included in it.

The first ~~or~~ Indian P. copoeia was published in 1868.

After independence an IP commity was constituted in 1948 which prepared IP in 1955.

P. copoeia contain western & traditional drugs

A new edition of IP has been published in 1996 has become effective from 1st December, 1996.

IP is a book of standard under the drug & cosmetic at 1940.

Features of Ist Edition of IP 1955

The title of monographs have been given in latin language

The english title has also been given below latin language.

The weight and measures have been given in matric system.

Doses are expressed in both matric and english system

The temperature has been expressed in Celcius

The descriptive terms (very soluble, freely soluble, slightly soluble, sparingly soluble) has been used were the exact solubility is not known.

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British Pharmacopoeia

The first pharmacopoeia to be published in Britain

was the 'Pharmacopoeia Londenises in 1684'

Other pharmacopoieas of importance in Britain were the 'Edinburg Pharmacopoeia' first published in '1699' and 'Dublin Pharmacopoeia' was first published in '1807'

In '1864' the fusion of the three pharmacopoeia resulted in the for publication of the 'British Pharmacopoeia'.

Since '1948' the British pharmacopoeia has been published at an interval of 5 year & to keep it up-to-date have been published at regular intervals.

The last edition of British P. copoeia is that '15th edition' published in two volume in year '1993'

It contain ~~21~~ '2040 monographs' each monograph sets out standard for medicinal of pharaceutical substance & preparation which are legally inforceable

United State Pharmacopoeia & National Formulary

The first edition of USP was published by 'United States Pharmacopeia Convention' on '15 Dec, 1820' in both language english & latin within its '272 pages' were enlisted '270 drugs' consider

It was decided to revise the p.copoeia in every 10 years. The conventant decided to revise it after every 5 years.

The first national formulary of U.S. was published by 'American Pharmaceutical Association' in '1888'

All drug substances and drug products ~~in~~ were covered in USP by pharmaceutical ingredients all excipients were covered in national formulary

It is used for determining the identity, strength, quality and purity of particles & specification for packaging & labeling

International Pharmacopoeia

The international pharmacopoeia first edition was published in '1951' by WHO

The 'second volume' of first edition was published in the year '1959'

The second edition published in '1967' was entitled - 'specification for quality control of pharmaceutical preparation'

The third edition was published in various volume under the title - 'The International Pharmacopoeia'. Volume I was published in '1979' & volume II in '1981'

International p.copoeia was defined as collection of standard which would serve as a refer reference for the establish of International standards.

Europian Pharmacopoeia

In '1964' the council of minister of Europian countries decided to establish a common p.copoeia

These countries Belgium, France, Neitherland, Italy, Germany & U.K.

The first volume of European p.copoeia was published in '1969', second vol. in '1971' & third vol in '1975'.

Extra / Martindale Pharmacopeia

The extra pharmacopoia was first produced in 1883 by William Martindale published by Royal Pharmaceutical society of great Britan.

The term extra means in this exctance outside because the book aimed to described drugs that were outside the British pharmacopoeia

It aims to provide practicing pharmacist physicians with up to date information of all drug substances, official and unofficial are contently used in pharmacy.

The Ist edition is entitled "The Extra Pharmacopoeia of unofficial drugs & Chemical & pharmaceutical preparation" was the slim pocket volume of 313 pages containing some 250 drug monograph.

Recently this pharmacopoeia has been made availble in the form of C.D., Data base form where information search it lot more easier.

National Pharmaculary

of India

The I^st national formulary of India was published by government of India in the year 1960.

The II^nd edition of national formulary in year 1966

It has been prepared with the aim to provide guidance to doctors, medical students and pharmacist in hospital.

The III^rd edition of national formulary contains 342 new formulation which were included in it.

The III^rd edition of national formulary in year 1979.

Pharmacy as a Career.

i- Production and manufacturing

ii- Formulation and development

iii- Quality assurance and Quality Control.

iv- Reasearch and development

v- Hospital Pharmacy

vi- Community Pharmacy

vii- Academics

viii- Marketing
- Sales promotion, manager, sales executive

ix- Government job
- Drug Inspector
- Drug controler
- Chemist shop.

x- Clinical research

xi- Cosmatic & food industries

xii- Pharmaclinic.

25/08

Academics

1- It is a full time fatilty member of an educational istitute i.e. university or polythekhic etc.

2. They are involved in teaching & learning of future generation of pharmacy.

3. Academic pharmaceutics in a university also engaged in researchs.

Pharmaceutical Marketing

Can also be defined as a management process that serves to identify and ~~nee~~ heal patient requirement in a proper way

Pharmaceutical business mainly adopt shelves and promotion of pharmaceutical products.

Chemist Shop

Pharmacy is a retailed shop with provides pharmaceutical & other product

Chemical Research

It is a branch of health care sciences that

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determine the effectiveness of medication, diagnostic product & treatement used for human.

Medical Coding

It is a translation of medical reports into a short code used within healthcare industry.

Editions of Indian Pharmacopoeia

Edition	Year
1	1955
2	1966
3	1985
4	1996
5	2007
6	2010
7	2014
8	2018
9	2022

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Chap-2
Packaging Material

1. Pharmaceutical containers has been defined as a device that hold the drug and it may or may not be in direct contact with the pharmaceutical preparation.

2. Closers are the device by means of which containers can be opened or closed.

3. Im - proper packing, poor quality of container can lead to deterioration.

Qualities of a good container

1. The container must not interact physically or chemically with the substance stored in it so as to change the strength, quality & purity of substance.

2. It should help in maintaining the stability of product against the environmental factors.

3. It should be made of material which can withstands wear & tear during normal handeling.

4. It should be designed that a dose can be withdraw from it conveniently.

5. The material used for making of containers must be non-toxic.

6. It should be withstand → changes pressure & temperature.

7. The container must be such that it can be labelled easily.

8. The containes must have the pharmaceutically eligent appearance.

9. The closer of the containes must be easily removable & replacable

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Types of Packaging

There are three types of packaging

1. Primary packaging - it is the material that first envelops the product & fold it.

This usually is the smallest unit of distribution and direct contact with the medicine

Eg- blister pack, alu-alu, aerozol bottles / spray.

2. Secondary packaging - it is outside the primary packaging used to group primary package together.

Eg- Box

3. Tertiary packaging - it is used to bulk handling and shipping.

It is in direct contact with the secondary packaging

Eg- Containers, cartons.

Types of Containers

Containers are divided into following types on the basis of there utility

1. WELL CLOSED CONTAINER

A well closed container protect the content from loss during transportation, handling & storage

2. SINGLE DOSE CONTAINER

These containers are used to supply one dose of medicament & hold generally parental product

Eg- ampule or vial

3- MULTI DOSE CONTAINER

a. These containers allow the withdrawl of ~~those~~ dose at various intervals without changing the strength, quality & purity of remaining portion.

b. These containers hold more than one dose & are used as injectables.
Eg- vials.

4- AIR TIGHT CONTAINER

a. These containers have air tight sealing and closing.

b. These containers protect the product from dust, moisture & air.

5- AMBER - COLOURED / LIGHT RESISTANT ~~ANCE~~ CONTAINER

a. These containers protect the medicaments from harmful effect of light or direct sunlight

b. These containers are used to store the photosensitive medicament.

6- AEROSOL CONTAINER

a. These containers are used to hold aerosol product.

b. These containers have adiquate mechanical strength in order to bear the pressure of aersol packing

Material used for making of container

The containes used for pharmaceutical are usually make from following basic material-

1. **GLASS**

Glass containers are very commonly used in pharmaceutical packaging.

- **Advantages of glass**

a. They are transparent
b. Glass are available in various shapes or size
c. They can withstand the variation in temperature and pressure
d. Glass materials are neutral after proper treatment.
e. They have good protection power
f. Glass material don't detaoriate with age.
g. They can be easily labelled and also attractive.
h. Glass containers can be sealed by removable & closer.

- **Disadvantages**

a. These are easily broken when dropped.
b. Glass containers are heavy wh with increases the transportation cos from one place to another

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- **Composition of glass**

a. Glass is composed of sand (SiO_2), soda ash (Na_2CO_3), limestone ($CaCO_3$)

b. Coiled material is broken glass i.e. mixed with the batched and act as fusion agent for the entire mixture.

The composition of glass varies & it depends on the specific purpose for which is used.

Silicon, aluminium, boron, sodium, potassium, calcium, magnesium, zinc, barium are generally used in preparation of glass.

- **Types of glass**

Glass can be following types which is used for making container of pharmaceutical product.

1. **Lime soda glass**

- it is composed of sand (SiO_2) 75%, (NaO_2) 15%, CaO (10%) along with some amount of K_2O, MgO and Al_2O_3
- it is not expensive and can be manufactured easily
- used for preparing container meant for storage of medicament.

- it is not suitable for parentral packaging because it liberate alkali in aqueous preparation, also it is not resistance to sudden changes, temperature and on repeated use it loses some of its brilliance

2. Borosil Glass
- it is composed of SiO_2 (80%), B_2O_3 (12%), Al_2O_3 (6%) & mixture of Na_2O, CaO and other oxides (2%)
- it is highly resistance.

3. Silicon Treated Glass
- Glass is treated with silicon so that it can be used for preparing container to store alkali sensitive product

4. Sulphured Glass
- it is a cheaper variety of glass used for contruction of glass for parentral product
- it doesn't react with alkali.

5. Neutral Glass
- it is composed of SiO_2 (72% - 75%), Na_2O (6% - 8%), B_2O_3 (7% - 10%), Al_2O_3 (4% - 6%), BaO (2% - 4%), K_2O (0.5% - 2%)
- it is resistant to alkali, weather and also withstand after auto-claving

- it is used for preparation of multidose, vials, ampules.

6. Amber Coloured Glass
- it is used for the stroge of photosensitive pharmaceutical product as it has the capacity to protect the product from UV radiation.

→ Following types of glass are used for preparation of container meant for storage of parentral product

1. Type I glass
also called as borosilicate or neutral glass.

2. Type II glass
it is a soda lime, silicate glass or it is used for acidic & neutral aqueous preparation

3. Type of III glass
it is also called soda lime, silicate glass.

it is suitable for non-aqueous sol.
eg- powder for parentral use

2. Plastic

Plastic containers are commonly used in pharma-

ceutical packaging

- **Advantages of plastic**

1. They are light in weight can be handle easily.
2. Plastic have sufficient mechanical strength.
3. They can be transported easily
4. They are unbreakable
5. Available is various shapes / size
6. They have good protection power.

- **Disadvantages of plastic**

1. They cannot withstand resistant heat without softening or distorting
2. Special types of gum or adhesive are required for labling.

- **Composition of plastic**

1. Plastic are synthetic polymers of high molecular weight
2. The adetives included in plastic material are anti-oxidant agent, lubricants, plasticizers, stabilizer.
3. The individual polymer has its own merits & demerits. Some of them are described.

a. **Polyethylen (polythene)**

(i) It is very flexible, very light plastic
(ii) It is impermeable to water vapour & does not deteriorats with age until exposed to direct sunlight for a long period.

(iii) It helps higher melting point & can be sterilized by auto clawing.

b. Polyvinyl chloride (PVC)

(i) It is less flexible, heavier and more permiable to water as compared with normal polythene

(ii) It is not effected by sunlight easily.

(iii) It is used for preparing eye ointment tube.

c. Polymethyl Methacrylate (PMMA)

(i) It is very hard, strong but light transparent / translucent plastic.

(ii) It soften add 100°C, it is used for preparing bottles & Tubes.

d. Polystyrene

(i) It is hard, rigid, light material.

(ii) They can be easily formed into any shape So it is used for preparing bottles, tube, jar, box & sirings.

e. Polytetra flouroethylene (PTFT)

(i) It is translucent, opaque, pulses and high resistance solvent & chemical.

(ii) It is unchanged even at temperature of 25°C
Eg - Chemical Bottles

f. Polycarbonate

(i) It is transparent, has high strength and good

heat resistance.

(iii) It is used in the preparation of surgical equipments

g. Polyamites (Nylon)

(i) It is very tough, plastic have great amount of flexibility & heat resistance.

(ii) Its melting point is about 200°C

(iii) It can be auto-play repeatedly.

(iv) It is used for the preparation of syringe & packing film or surgical dressing and instruments.

- Classification of Plastic

Plastics are classified into two groups acc. to their behaviour when heated.

(i) Thermoplastic - This type of plastic gets soften to a viscous fluid on heating and hardens again on cooling.
Eg - Nylon, Polystyrene and Polymethyl Methacrylate.

(ii) Thermosetting plastic - This type of plastic may become flexible but does not become fluid on heat
Eg - Resins, formaldehyde.

3. Metal

(i) Metals are used for the construction of containers.

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(ii) Tin, Sc, Al, Pb are the most popular metals correctly used in pharmaceutical packaging.

- Advantages of metals

(i) They are impermeable to light, moisture & glass.
(ii) They can be make into rigid unbreakable container.
(iii) They are light in weight as compared to glass container.
Labels can be printed directly on to their surface

- Disadvantages of metals.

(i) They are more expensive.
(ii) The metal containers are also used for bulk packaging of tablet, food, powder and food material.
(iii) The collapsible tube make for the are prefered because they are compatable with wide range of product, they are quite costly.
(iv) The colaxible tube made from aluminium are light in weight & normally used for toothpaste and creams.
(v) (Pb) head tubes are the cheapest among all the metals but are not used for pharmaceutical packaging due to lead poisoning.

Rubber

It is an excellent material for foaming seals used to form closure of vials & in other application such as gased in aerosol.

- Categories of Rubber

(i) Natural rubber - (a) suitable for multiple use for closure for insectable product.

(b) The disadvantage is that it does in well tolerate multiple auto claving & these become brital.

(c) There is a risk of product absorbing.

(ii) Synthetic rubber - (a) They contain additives.
Eg - Butyl, Chlorobutyl

(b) Softer rubber experience better recieving while harder rubber are easier to process on packing lines.

01/09

Chap-3 Pharmaceutical Aids

1. The substance which have little or low therapeutic value but essentialy used in manufacturing of various pharmaceuticals in order to provide bulk, strength, stability, good texture & proper shape or size, along with colour & flavour are known as pharmaceutical aid.

2. They are not API.

3. They may be obtained from natural sources (vegetable, animal or mineral) or can be chemically synthesised.

Types of Pharmaceutical Aids

1. Colouring agent
2. Sweeting agent
3. Flavouring agent
4. Preservative
5. Suspending agent
6. Emulsyfing Agent
7. Disintegrating agent
8. Dilluents

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1. COLOURING AGENT

a. Colourents or colouring agents are mainly used to impart a distinctive appearance to the pharmaceutical doses form.

b. We can also say that colourents are the cosmetics for pharmaceutical preparation because the asthetic appearence of doses form can be ~~it~~ enhanced by using suitable colour.

● Pharmaceutical preparation are coloured for the following reason-

a. Increase Acceptibility - Unattractive medicine can be made more acceptable to the patient by use of colour

Colour can also be used to make a preparation more unique

b. Identification - It helps to identify a product in manufacturing

Use of different colour for different strength of the same drug can also helps to eliminate error.

c. Stability Purpose - Some of the insoluble colour or pigment when used in tablet coating can contribute to the stability of light sensitive material.

Ideal properties of colourants:-

a. Colourant should be non-toxic
b. Free from harmful impurities
c. The colouring agent have high strength so that
d. only small quantities are required.
e. Unaffected by oxidising & reducing agent
f. Compatible with other medicaments & excipients and not interfere with them.
g. Free from objectionable taste or odour.
h. The colouring power of colourants must be reliable
i. Unaffected by light, temperature & microorganism & must be stable on the storage

Classification of Colourants

1. Organic dyes.
2. Inorganic or mineral colour
3. Natural colour

1. **Organic dyes** – Dyes are synthetic chemical compound that exibhit their colouring power when dissolve in a solvent.
   Eg- Tartazine (lemon yellow)
   Patent Blue -V
   Erythrosine (pink colour)

2. **Inorganic or Mineral Colour** – Stability towards light is the most important characteristics displayed by these colour.
   Eg= Titanium oxide

2. The important application in present days is the use of the mixture of red & yellow ferric oxides to give calamine a flesh colour.

3. Titanium oxide is used to cover hard gelatin capsule.

2. NATURAL COLOUR

a. Some of these colour are product of chemical synthesis rather than extraction from natural sources.
Eg- β- Carotene

b. Natural colours are not stable to light as a other group of colour.

c. However, they have a wide range of astability

03/09

2. FLAVOURING AGENT

a. Flavouring agent is the substance which provides an intrisic flavour to a formulation.

b. It mask the unpleasant taste (bitter taste) & chance patient acceptibility by the use of different flavours.
Eg- an organe mint flavour is especially used in diphenhydramine expectorant

- Types of flavouring agent:

1. Salty flavour - Butterskotch and Vanilla

2. Bitter taste - walnut, mint, chocolate

3. Sweet flavour - berry, mango and strawberry

4. Sour taste - orange, lemon

5. Preffered flavour -

(i) Antibiotics - Cherry, pineapple, orange, cinnamon, strawberry

(ii) Anti-histamines - (used to reduce / prevent allergic rxn) Apricot, orange, honey or raspberry

(iii) Barbiturates - (drug used to reduce working of CNS) Banana, pineapple, cinnamon, pepper mint, orange

(iv) Expectorants - (used to get relief in cough) Apricot, strawberry, lemon, coriander or pineapple

(v) Electrolyte solution - Cherry, grapes, strawberry or gooseberry.

~~(vi) Vanillin~~

A. Vanillin

- Chemical name - 4- hydroxy - 3- methoxy benzaldehyde
- Description - white or cream colour, crystalline power with characteristics vanilla flavour & salty taste

- Functional category - flavouring agent
- Application - Vanillin is used as a flavour in food & pharaceutical formulation
- Method of manufacture -

(i) It occurs naturally in many essential oil & particularly from the buds of 'vanilla planifolia'

(ii) Industrially vanillin is prepared from lignan

(iii) lignan is treated with alkaline & elevated temperature in the presence of catalyst to form a complex mixture of product from which vanillin is isolated

(iv) It is then purified with recrystallisation

3. SWEETING AGENT

To increase the acceptibility of the doses form & mask the ~~up~~ unpleasant taste of API in formulation

The main sweeting agent include in oral preparation are - sucrose, liquid glucose, glycerol, sorbitol, sacrin sodium & Aspartame.

Generally used in solid oral & liquid oral preparation.

Used in formulation - chewable tablets, oral suspension, oral solution

a. Saccharin sodium

Functional category - sweeting agent

→ Application in pharmaceutical formulation -

1. Saccharin Na is an intense ~~sweett~~ sweeting agent used in beverages, food product, tablet, tablet sweetner & pharmaceutical formulation such as tablet, powder, gels, suspension & mouth washers.

2. it is also used in vitamin preparation.

3. Saccharin sodium is generally more soluble in water than saccharin & is more frequently used in p. ceutical formulation.

4 its sweeting power is approximately 300 to 600 times than sucrose.

5. Saccharin sodium enhances ~~the~~ flavour and mask some ~~up~~ unpleasant taste

04/09

Preservatives

1. Preservatives are the substance which are pharmaceutical product to inhibit the microbial growth.

An ideal preservative would be effective at low concentration against as possible microorganism.

→ Ideal properties of preservatives

1. It should be non-irritant
2. It should be non-toxic
3. It means to be chemically or physically stable.
4. It should be compatible with wide range of ingredients.
5. It should be act as anti-microbial agent.
6. It should be effective in a small concentration.
7. It should maintain activity throughout product manufacturing shelf-life and uses.

→ Classification of preservatives.

A. Classification based on mechanism of action

1. Anti-oxidant
   Vitamin E and Vitamin C
2. Anti-microbial agent
   Sodium benzoate, benzoic acid, Sorbide.

B. Classification based on sources

1. Natural preservative
   Neem oil, salt, lemon, honey

2. Artificial preservative
Sorbide, benzoic acid, nitrile

→ Mechanism of action
1. Natural substances such as salt, vinegar, used as traditional preservative.

2. Ascorbic acid and citric acid inhibit the action of enzyme.

→ Preservatives and there uses

A- Benzoic acid
It inhibit the growth of yeast and some bacteria also used as antiseptic.

B. Boric acid
used as antiseptic

C. Ethyl paraben
used as preservative and food ~~att~~ additive

D. Microbial compound.
used as bacterial preservative and topical antiseptic

E. Achhol ~~thor~~ chlorobutenol.
used as preservative in various pharamaceutical like solution, specially injectibles

08/09

Chap-4
Unit Operations

1. Size Reducteon

It is the process of reducing drugs plants or Chemical substances in small pieces, coarse powder or fine powder.

- Importance of size reduction.

1. To increase the rate of solubility.
   to allow the rapid penetration of solvent during extraction
2. To get a uniform powder because ~~reducde~~ reduce particle size help in ~~gt~~ getting uniform mixing of drug.
3. To increase the rate of absorption
4. To improve the stability of certain pharaceutical dose form like suspension.
5. To help in the process of separation of solid from liquid by filteration

- Factor affecting of size reduction

1. Hardness - It is easier to break soft material to small size than hard material.

2. Toughness- Crude drugs are made of fibre on dose ~~fro~~ having higher moisture contain

are generally tough in nature
b. A soft but tough material may present increase the more problem in size reduction

3. Stickness - It is difficult to powder a drug having gummy nature because the material adare to the grinding surface.

- Material Structure -
Material which show some special structure may cause problem in size reduction.

- Moisture Content -
a. The material should be either dry or wet.
b. The material having 5% moisture in case of dry grinding and 50% in wet grinding does not create ~~size~~ any problem in size reduction.

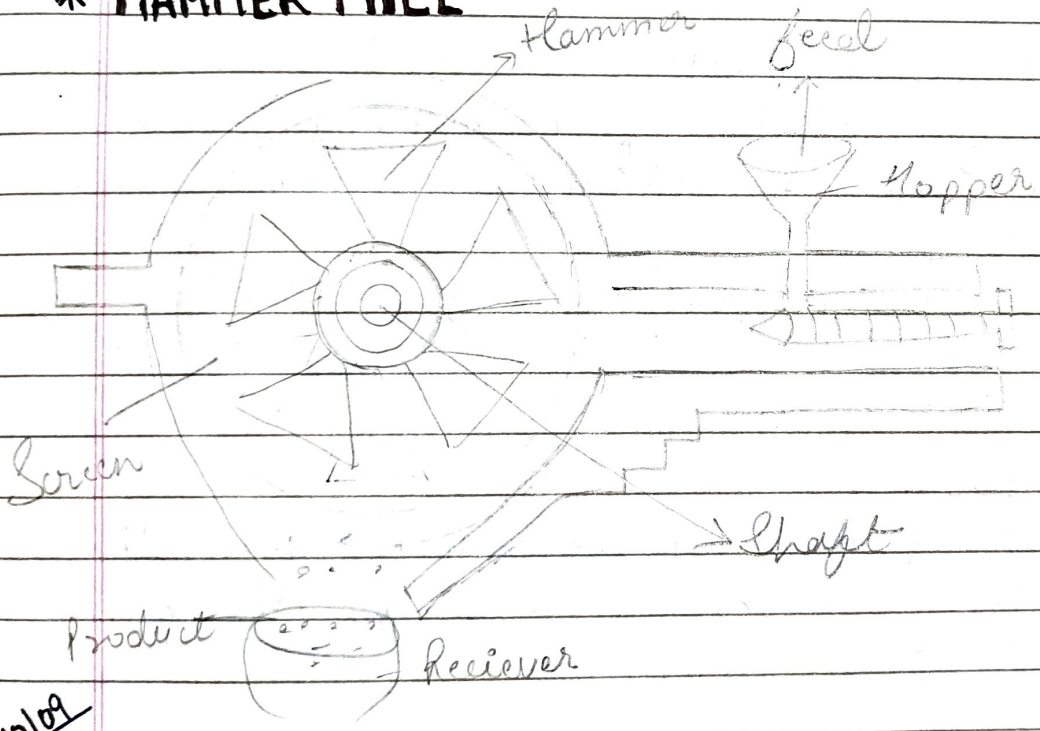
- ~~Softing~~ Temperature
a. Waxy substances such as sterric acid or drug containing oil or fat becomes soft during size reduction as heat is generated.

- Purity required -
Various mills used for size reduction often leaves some of the content & dust impurities come in the powder.

- **Physiological effect**
  Some drugs are very potent during there size reduction in a mill, dust is produced with may have an affect on operater.

- **Bulk density**
  The output of size reduction in a machine depends upon the bulk density of the substance.

* HAMMER MILL



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- **Principle**
  It works on the principle of impact material is Material is more or less stationary & is hit by hammer, moving object at a high speed.

- **Construction.**

1. It contains a jacket wall, enclosing a roller shaft to which four or more swinging hammers are attached.

2. The lower part of the casing consist of a screen from which material can pass & collect in a suitable reciever

3. When the desired degree of size reduction is reached.

- **Working**

1. The material is put into the hopper which is connected with drum

2. The material is powdered to the desired size, due to fast rotation of hammer, the material is collected under the screen

3. The mill can produce coarse to moderate fine powder.

- **Advantages**

Continuous operation can be done because the chance of jamming is less as the hammers are not fixed.

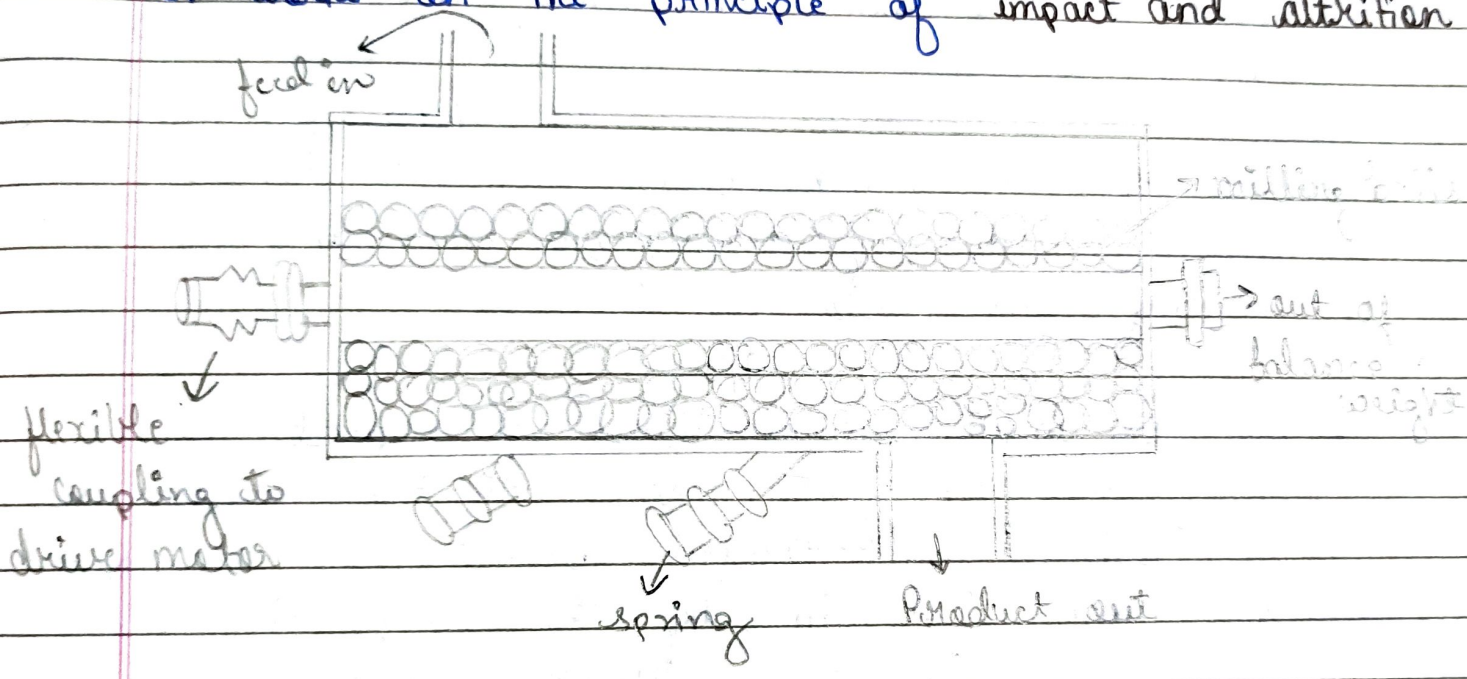
- **Disadvantage**

1. Cannot be used for fibrous product
2. Due to high speed of operation heat is generated which may effect ~~their~~ thermolabile drug or material
3. High speed of operation also causes damage to the mill if foreign obj. such as stone or metal is present in the feed

- **Uses-**
  It is used for producing intermediate grains or powder from almost all types of substances except sticky material.

→ BALL MILL

- **Principal**
  It works on the principle of impact and attrition



- **Construction**

1. It consist of a hollow cylinder which is mounted on the metallic frame that it can be rotated on its longitudinal axis

2. The cylinder contains balls that occupy 30% – 50% area of the main volume

3. The ball size depends upon the size of feed and the diameter of mill

4. The cylinder and balls are made of metal and lying

lined with rubber.

- **Working-**

1. The drug be grounded is put into the cylinder and is rotated.

2. The speed of rotation is very important factor in ball mill, at low speed the balls will slide & roll over each other and only negligible amount of size reduction will occur.

3. At high speed, the balls will be thrown at the walls by centrifugal force and no grinding will occur.

2/3

4. But at about second thirad of speed the centrifugal force just occurs with the result that the balls are carried almost to the top and then fall in by this way the max. amount of size reduction will occur

5. After a suitable time the material is taken out & passed to a seive to get powder of required size

- **Advantage**

1. It can reduce very fine powder
2. It is suitable for both dry & wet grinding process.
3. It can be used to grind toxic substances because the mill is totally closed

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4. It is capable of grinding a large variety of different degree of hardness.

- **Disadvantage**

1. The ball mill is very noisy machine
2. Ball mills are very slow due to grinding

- **Uses**

1. It is used to grind brittle drug to fine powder

2. Size Separation

The process of size reduction is followed by size separation of the powdered material.

A special technique is used to separate particles of specified size which is known as a process of size separation.

- **Objectives of size separation**

1. To increase the solubility
2. Selection of powder for manufacturing the tablet and capsule.
3. To increase the absorbtion

- **Official grades of powder.**

The Indian Pharmacopoeia – has led down the standards for powder for pharmaceutical purpose.

It specifyes five grades of powder -

~~Coarse powder~~

1. **COARSE POWDER** 10/44

A powder of which all the particles passed through a sieve with nominal mesh aperture of 1.70 mm (micrometre) (sieve no. 10) and more than 40% through a sieve with nominal mesh aperture of 355 µm (sieve no. 44) is called coarse powder.

2. **MODERATELY COARSE POWDER** 22/60

A powder of which all the particles passed through a sieve of nominal mesh aperture of 710 mm (sieve no. 22) and not more than 40% through a sieve with nominal mesh aperture of 250 µm (sieve no 60) is called moderately coarse powder.

3. **MODERATELY FINE POWDER**

A powder of which all the particles pass through a sieve of nominal mesh aperture of 355 µm (sieve no. 44) and not more than 40% through a sieve with nominal mesh aperture of 180 nm (sieve no. 85).

4. **FINE POWDER**

If all the particles passed through a sieve of nominal mesh aperture 180 nm (sieve no. 85) is called as fine powder.

5- **VERY FINE POWDER**

If all the particles pass through a sieve of nominal mesh aperture of 125 nm (sieve no. 120) is called very fine powder

→ Grades of powder and sieve through pass

	Grades of powder	Sieve through which all particles must pass	Sieve through which not more than 40% powder can pass
1.	Coarse powder	Sieve no. 10	Sieve no. 44
2.	Moderately coarse powder	sieve no. 22	sieve no. 60
3.	Moderately fine powder	sieve no. 44	sieve no. 85
4.	Fine powder	sieve no. 85	—
5.	Very fine powder	sieve no. 120	—

Sieves

1. Sieve or pharmacopial testing are constructed from wire with square mesh, woven from ~~the~~ wires of bronze, stainless steel or any other suitable material.

2. The wire should be uniform circular cross section

3. There should not be any reaction b/w the material of sieve & the substance which is passed from it

- **Standards for sieve.**

Sieves used for pharmacopial testing must specify the following.

1. **No. of sieve**

Sieve number indicates the no. of mesh in a length in each transverse direction parallel to the wire A number indicates the no. of meshes in a given length (2.54 cm ~~for~~ or 1 inch)

2. **Nominal Size of Aperture**

It indicates the distance b/w the wires.

3. **Approximate % sieving area.**

This expresses the % of total area of the sieve & the area of mesh
The ratio of total mesh area to the total sieve area

4. **Nominal diameter of wire.**

Wire mesh sieve are made from the wire having specified diameter in order to give suitable aperture size
The specified diameter of the wire used to construt the sieve

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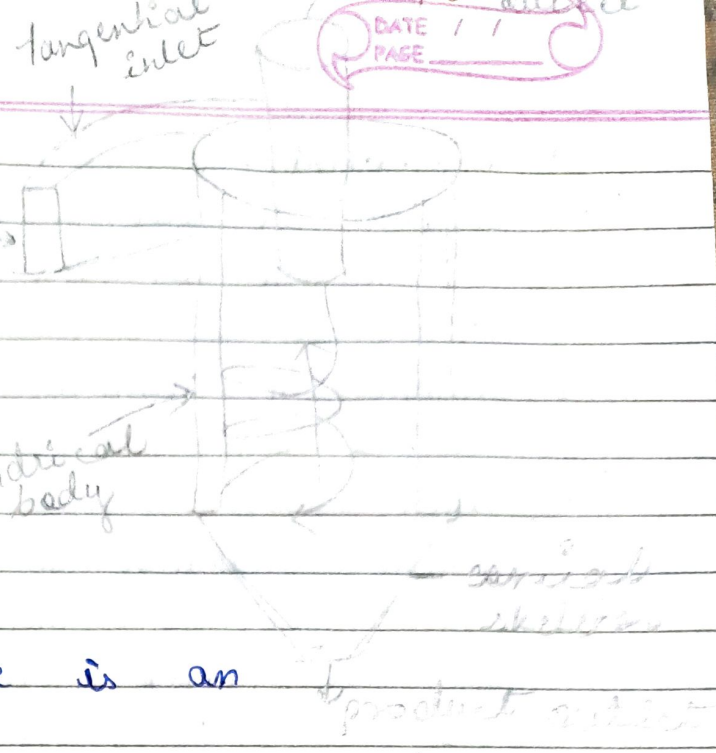
1. **Cyclone separator**

- **Principle** it works on the principle of centrifugal force.



- **Construction**

1. It consist of a cylindrical vessel with a conical base

2. In the upper part of the vessel there is an inlet and outlet

3. And at the base there is an another outlet

- **Working**

1. Suspension or mixture is introduced at a very high velocity so that rotatory movement takes place within the vessel.

2. The fuel or smaller particles are removed from the central outlet at the top

3. The heavy particles are removed by the outlet at the base

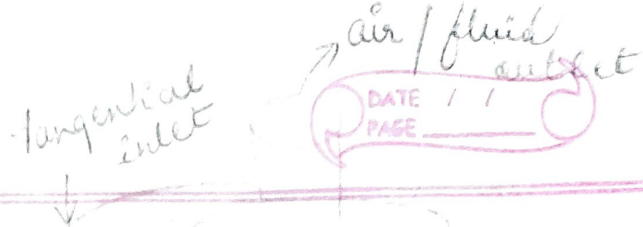
- **Advantage**

1. ~~No~~ less capital cost

2. It is small related to other separation equipm.

3. No moving parts

4. Can operate a pressure



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2. The fuel or smaller particles are removed from the central outlet at the top

3. The heavy particles are removed by the outlet at the base

- **Advantage**

1. ~~No~~ less capital cost

2. It is small related to other separation equipm

3. No moving parts

- **Disadvantage**

1. Difficult to obtain good separation of substance of similar densities
2. Unable to separate sticky material

- **Uses**

1. Cyclone separator used to separate mixture of solid particles, the suspension of solid in gas and liquid suspension with solid

3. # Mixing

Mixing is the most widely used operation in which two or more than two substances are combined together is called as mixing

- **Objectives**

1. Simple mixing of material to form a uniform mixture.
2. To promote the chemical reaction to get uniform product
3. Dispersion of solid in liquid to form suspen. or paste.
4. Dispersion of two immiscible liquids to form emulsion

- **Types of mixtures**

1. **Positive mixtures**- When two or more than two miscible liquids or solid soluble is dissolve in water, the mixtures are called positive mixture.
It is also called as non-reversible mixture.

2. **Negative mixture**- When two or more immiscible liquid are mixed or insoluble solids are mixed with water it forms negative mixture

3. **Neutral mixture**- These mixtures are static in there behaviour.
The substances do not have that tendency to mix with each other immediately, but once they are mixed then they cannot be separated.

- **Mechanism of mixing**
Convection mixing
Diffusive mixing
Shear mixing

1. **Convection mixing**- There is a bulk movement of group of particles from one side of powder to another
It occurs by an inversion of powder by means of blade or padle, it is called as convection mixing

2. **Diffusive mixing**- It occurs when random motion of particles within a powder pad causes them to change position related to one another is called as diffusive

3. Shear mixing- When shear forces occur it reduces the segregation and do the proper mixing.

- Factor affecting the perfect mixing of powder

1. Particle size- the variation of particle size can lead to separation because the smaller particles move downward to the spaces than bigger particles
Size of particle ↓ ∝ ↑ Mixing

2. Particle shape- The ideal particle is spherical in shape.
The irregular shape can become interlock and can affect proper mixing
Spherical shape particle ∝ ↑ Mixing

3- Proportion of material- The best result can be achieved if two powders are mixed in equal proportion by weight or by volume.
Equal material proportion ∝ ↑ Mixing

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4. Material density- Dense material always moves downward therefore proper attention should be given to the density by mixing.

Light weighted particles are easily mix in compression to heavy weight particles

- Equipment used in mixing-

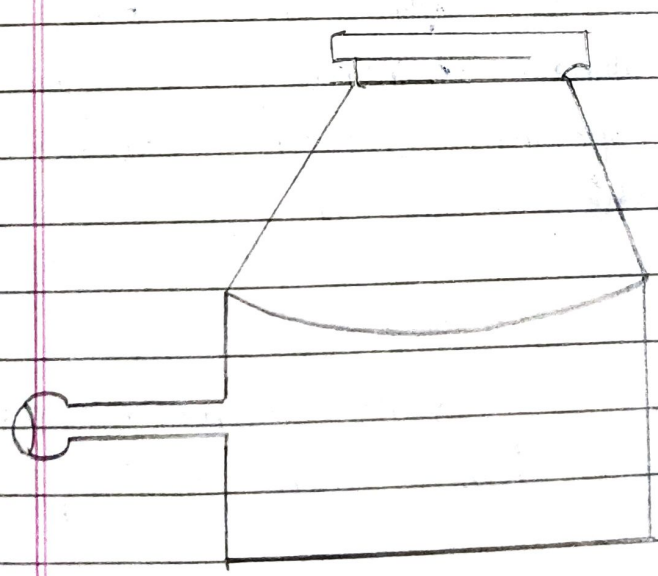
1. Mixing of powder- double cone blender, Tumbler mixer, air mixer for powder mixing.

2. Mixing of liquid- Turbine, mixer, propeller mixer, paddle mixer

3. Mixing of semi- solid- Triple roller mill, agitator mixer, planetary mixer.

4. Chromo _____ - silver mixer, hand homoganizer, colloidal mill

1. DOUBLE CONE BLENDER



- **Principle-**
It works on the principle of tumbling motion and axial rotation

- **Construction -**

1- **Conical vessel-** The blender is comprised of to cylindrical cones.

2- **Electric motor-** A motor drives the rotation of the blender.

3. **Stand & Support-** A bowl wearing stand supports the entire assembly.

4- **Loading or discharge cone-** Open in or present on both its from one opening we can feed the material & from second opening we can discharge the material.

- **Working-**

1. The mixing of powder in double cone blender is due to shearing action with plate / blade

2. It is made up of stainless steel & is availble in different capacity from 5Kg to 2Kg ~~on~~ or even more

3. The effency of blender depends mainly on the speed of rotation 30 to 100 ~~op~~.

4. The material to be blend is located approx.

50 to 60% of total capacity of the blender

5. As the blender rotates the material under those tumbling motion & mixes the material.

6. Once the desired level of blending is achieved the rotation is stop. The material is than discharged

- **Advantage**

1. Maintainance is easy
2. Uniform mixing is done
3. Large amount of material can be handle easily.

- **Disadvantage**

1. It required large space
2. It isn't suitable for particles with greater size.

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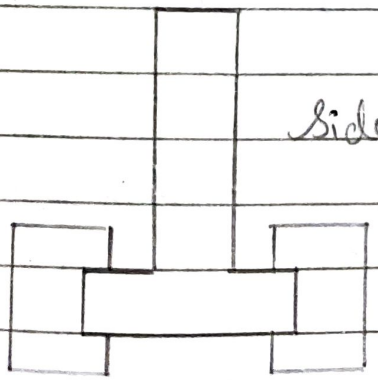
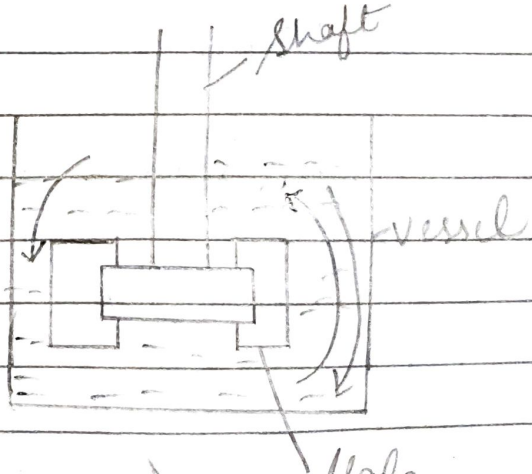
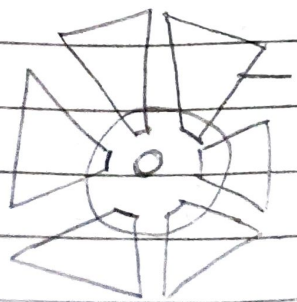
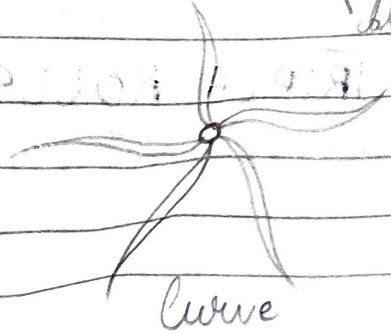
1. TURBINE MIXER

- **Principle** - It works on the principle of centrifugal force at rotational movement









- **Working and Construction**

1. It consist of a vessel and circular disc emperor
2. A number of shaft, straight, curve blades are attached to it.
3. The turbine is usually rotated at lower speed.
4. The mixer is used for mixing of viscous liquid Eg- syrup, liquid paraffin, glycerine etc.

- **Advantage**

1. Effective for high viscous solution.
2. They can handle slurries with 60% solid.

- **Disadvantage**

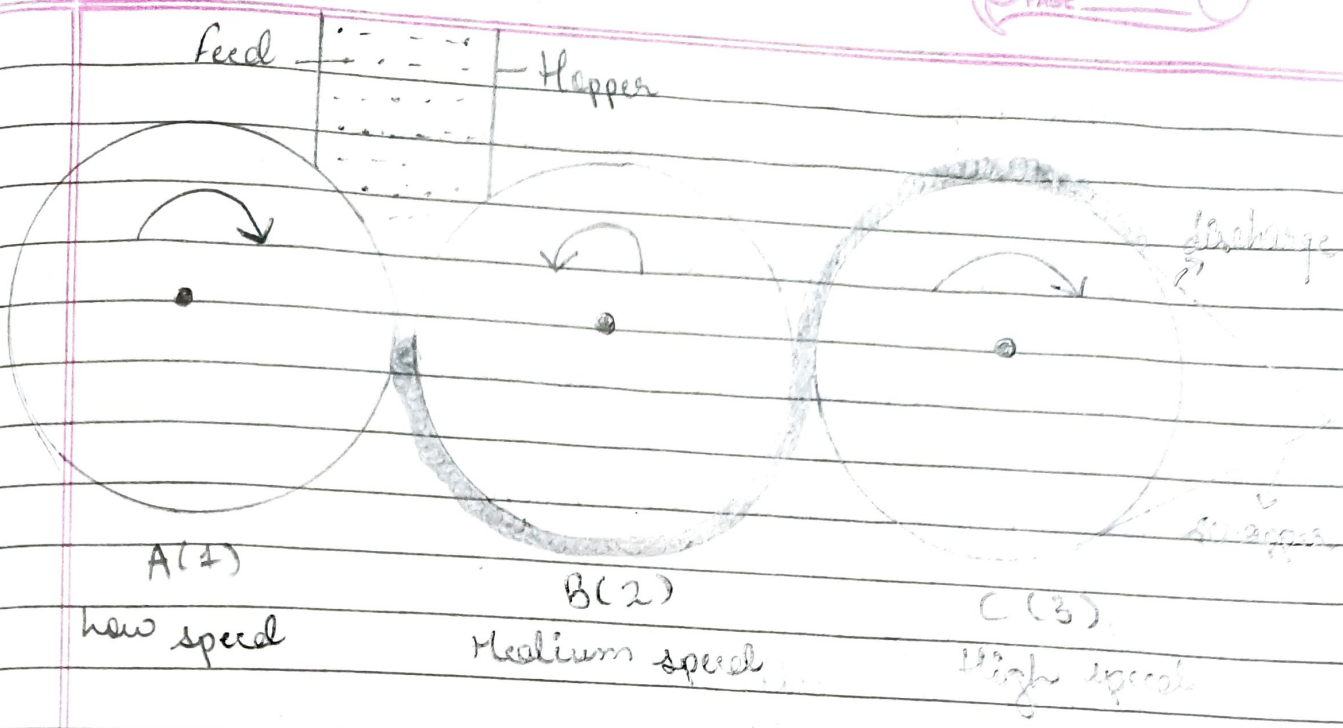
1. It is operated at very low speed so that it is very time taking process.
2. Higher cost as compared to other methods.

- **Application or Uses**

1. It is used for making of emulsion and suspension.
2. Also used for mixing of syrup and glycerine

2. TRIPLE ROLLER MILL

- **Principle-** It works on the principle of high shear which causes crushing of material.



- **Construction**

1. The mill consist of three rolers which are made of hard abrasive material.

2. These rolers are rotated at different speed.

3. The material coming b/w the roller is crushed depending on the gap b/w them.

- **Working**

1. The material after passing through the hopper comes b/w roller 1 and 2 and is reduced in the ~~side~~ size process.

2. The gap b/w roller 2 & 3 is quite less than 1 & 2, further crushes it and smooth the mixture which adares to roller 2

3. Scrapper is arranged in such a way that it can remove the mixed material from roller 3.

- **Advantage**

1. Continuous operation is possible.
2. High shear applied.
3. Size reduction is possible.
4. Mixing efficiency is high

- **Disadvantage**

1. Washing is difficult.
2. High power consumption.
3. High operation cost
4. There is risk of contamination.

Filteration

The process in which heterogenous mixer of fluid and solid particle are separated by the filter medium ~~or~~ which permit the ~~passi~~ passage of fluid but retains the solid particles is it termed as filteration

- Basic Terms used in filteration-

1. Slurry -: The material to be filtered is called as slurry

2. Funnel -: It is an instrument in which filteration process is done is called as funnel.

3. filter medium -: The coarse medium used to retain the solid is called as filter medium.

4. Filter cake ~~of~~ or filter bed- The solid particles accumulated on the filter medium is called as filter cake.

5. Filterate- The liquid passes through the filter media & collect in the container is called as filterate.

- Objectives & Applications

1. To separate the solid & liquid mixture

2. To clarify the liquid.

3. To remove the contamination of liquid.

4. Formulation / production of liquid oral formulation.

Driving force-
It is defined as the slurry is filtered out by which force is called driving force which can be increased or decreased

driving force = pressure upstream - pressure downstream

- Theory of filteration through
The liquid flowing to a filter medium follows the basic rule governing the flow of any liquid through a medium which offer resistance

$$\text{Rate of filteration} = \frac{\text{driving force}}{\text{resistance}}$$

Theory of filteration can be explained by the following equation

a. Poisseuleis equation
b. Darcy's equation
c. Kenzey carman's equation

A. POISSEULEIS EQUATION

Poisseuleis consider that filteration is similar to the streamline to the flow of liquid under pressure through the capillaries

$$V = \frac{\pi \Delta p r^4}{8 l \eta}$$

V = rate of flow
ΔP = pressure difference across the filter

rate of flow decrease with decrease in filteration

l = thickness of the filter cake
η = viscosity of the filterate
r = radius of the capillary in the filter bed.

B. DARCY'S EQUATION

The factor influencing the rate of filteration has been incorporated into an equation

$$V = \frac{KA\Delta P}{\eta l}$$

K = permeability coefficient of the cake
A = surface area of the filter medium
l = thickness of filter cake
η = viscosity of cake
ΔP = pressure difference across a filter
V = rate of flow.

C. KOZENY CARMAN'S EQUATION=

This is the resultant equation of poiseuille's Darcy's which is widely used in filteration

$$V = \frac{A}{\eta s^2} \times \frac{\Delta P}{Kl} \times \frac{\varepsilon^3}{(1-\varepsilon)^2}$$

s = surface area of particles comprising the K
K = Konzey constant
ε = porosity of the K
l = thickness of filter cake

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- **Factor influencing filteration**

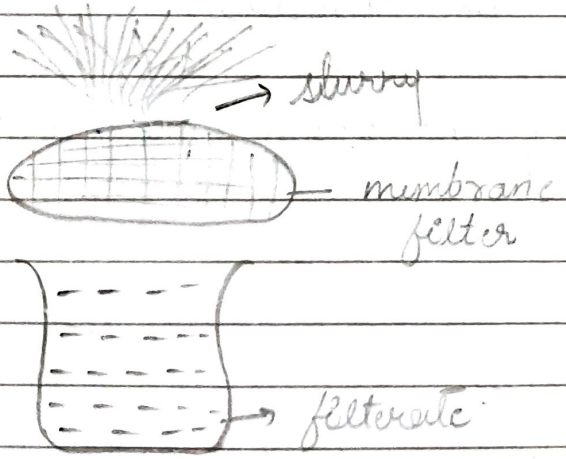
1. Surface area of filter medium can increase the flow of filteration.

2. Filter cake resistant = increased filter cake $\propto \frac{1}{\text{rate of filteration}}$

3. Increased viscosity $\propto \frac{1}{\text{rate of filteration}}$

A. **Membrane filter**

- **Principle-** it work on the principle of surface filteration i.e. larger particles are retained on the surface of the filter.



- **Construction-**

i- Membrane filter is made up of thin & flat membrane of cellulose derivatives such as cellulose acetate & cellulose nitrate.

ii- The filter are brittle when it dry condition but they have strength when it is in wet condition.

iii- The membrane filter are 50 - 150 μ (micron) & available in the size of 60 cm^2

- Working-

i- Membrane filter consist of 400 - 500 million pores per sq. cm of filter surface

ii- The pores are uniformly distributed in size & occupy 80% area of filter volume

iii- When slurry is pored down to the membrane it allows liquid to pass & solid to resist in this way liquid is separated out.

iv- The selection of the membrane filter depends upon the particles to be removed

v- To avoid clogging of membrane pre-filter is often required

- Advantage-

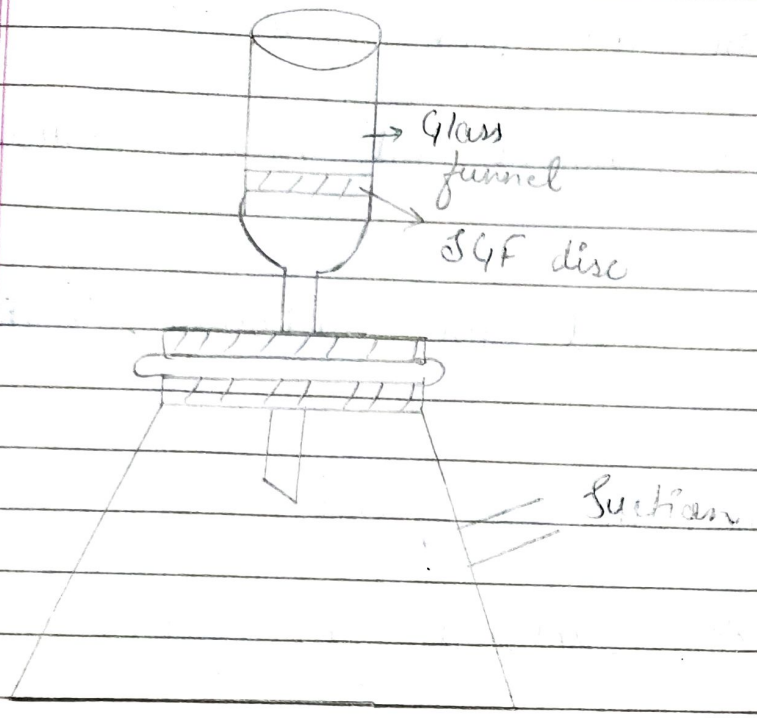
1- It is a rapid process

2- These are available as disposable items & hence contamination is prevented

- Disadvantage-

1. It cannot be used for filteration of organic solvent such as alcohol, chloroform, Ketone etc.

B. Sintered Glass Filter.



- Principle- it works on the principle of surface filteration

- Construction-

1. These are made up of borosilicate glass.
2. Borosilicate glass is finely powdered, sieved and particles of desired size is separated.
3. It is packed into disc mold & heated to a temperature at which adation takes place b/w the particles.
4. The disc is then fused to a funnel of suitable shape & size.
5. The centered glass filter are available in different pore size.

6. Hence, the funnel with a centered filter is numbered acc. to the pore size.

7. The filteration is carried out under reduced pressure.

8. These funnel are used for bacterial filteration.

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- **Working-**

1. Take the mixture to be filter.

2. Pass it through the sintered glass filter under reduced pressure.

3. Particle larger than pore size retained on the surface of filter.

4. Liquid pass through the sintered glass filter.

5. Collect the filterate in suitable container.

- **Advantage-**

1. Easy to clean.

2. A very small quantity of medicament is absorbed on the surface of filter medium.

3. It can operate with pressure.

- **Disadvantage-**

1. They are expensive

2. They are fragile & time taking.

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Drying

1. Drying is an important technique used in pharmaceutical chemistry.
2. It is defined as final removal of moisture from solid by vaporisation with the help of heat.

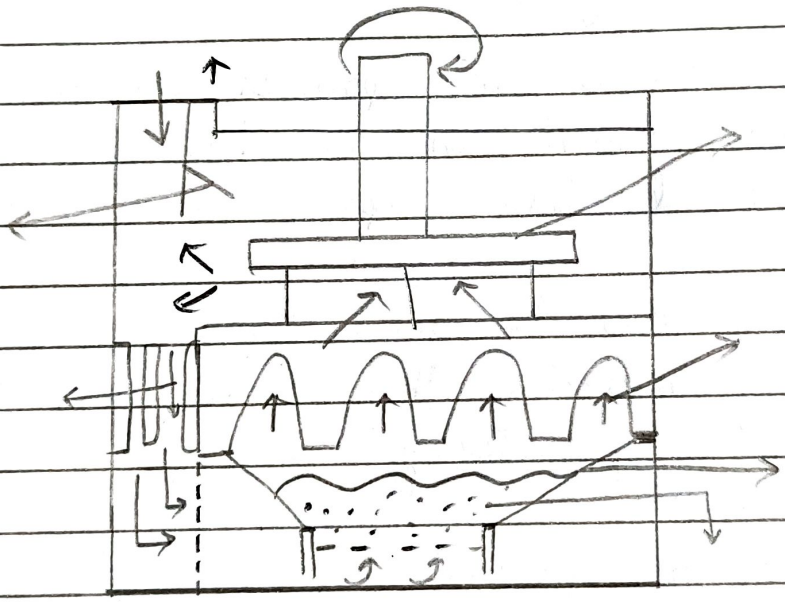
- **Application of drying**

1. It is used as a unit process in the manufacturing of granules which can be despressed in bulk or converted into capsule or tablet
2. Drying can also be used to reduce the bulk & weight of material thereby lowering the cost of transportation & storage.
3. It helps in the prevention of crude drugs of plant from bacterial growth which occurs due to presence of moisture.
4. It helps in the size reduction of crude drugs, the presence of moisture in the crude drug does not allow it get powdered easily
5. Drying is also used in the processing of materials Eg- preparation of dried $Al(OH)_2$, spray drying of dextrose & in the preparation of solid extract

- Equipments used in drying process

1. Tray dryer
2. Turner dryer
3. Rotatary dryer
4. Fluidized bed dryer
5. Freeze dryer

1. FLUIDIZED BED DRYER



- Principle - Fluidisation the solid particles are suspended into air

In fluidized bed dryer, good contact b/w hot air & particles to be dried is obtained which causes ~~repeated~~ rapid drying.

- Construction -

1. The dryer is made up of stainless steel.

2. A detachable bowl is placed at the bottom of the dryer which is used for loading & discharging.
3. The bowl has a perforated bottom with a wire mess support for placing the material to be dried.
4. A fan is mounted in the upper part for circulating hot air & maintaining the pressure.
5. Fresh air inlet & heat exchanger are connected serialy to heat the air to the required temperature
6. Back filters are placed about the drying portal for recovery of fine materials / particles.

- **Working -**

1. The base of the container filled with material is heated with hot air stream.
2. The fresh air is suck using a blower & it is heated by electrical heaters.
3. The hot air expands into bed of material & create a dry atmosphere
4. This phenomena is known as fluidization

- **Advantages**

1. It gives a high drying rate in comparison to other drying method (tray dryer)

2. The method is suitable for thermolabile substances because heating time is minimised.

3. The FBD & takes place from individual particles & heat from the entire bed.

4. The temperature inside the FBD can be controlled & uniform.

5. The FBD has a high output & occupy small floor space.

- Disadvantages

1. The turbulance produce when hot air is passed through the material may cause attrition to some particles - which leads to the production of fine particles.

- Uses -

1. It can be used for drying of any powdered material but mostly it is used for drying of granules made for manufacturing of tablet.